## P. ENT COOPERATION TREAT

	From the INTERNATIONAL BUREAU		
PCT	То:		
NOTIFICATION OF ELECTION  (PCT Rule 61.2)	Assistant Commissioner for Patents United States Patent and Trademark Office Box PCT Washington, D.C.20231 ETATS-UNIS D'AMERIQUE		
Date of mailing (day/month/year)			
21 July 2000 (21.07.00)	in its capacity as elected Office		
International application No. PCT/GB99/04013	Applicant's or agent's file reference REP06284WO		
International filing date (day/month/year)	Priority date (day/month/year)		
01 December 1999 (01.12.99)	01 December 1998 (01.12.98)		
Applicant			
HART, John, Ernest			
in the demand filed with the International Prelimina  21 June 2000  in a notice effecting later election filed with the International Prelimina  22 June 2000  in a notice effecting later election filed with the International Prelimina  23 June 2000  in a notice effecting later election filed with the International Prelimina  24 June 2000	0 (21.06.00)		
was not	· ~		
made before the expiration of 19 months from the priority Rule 32.2(b).	v date or, where Rule 32 applies, within the time limit under		
The International Bureau of WIPO	Authorized officer		
34, chemin des Colombettes 1211 Geneva 20, Switzerland	Zakaria EL KHODARY		

Telephone No.: (41-22) 338.83.38

Form PCT/IB/331 (July 1992)

Facsimile No.: (41-22) 740.14.35



# PCT

(PCT Article 18 and Rules 43 and 44)

INTERNATIONAL SEARCH REPORT

Applicant's or agent's file reference	FOR FURTHER see Notification of	of Transmittal of International Search Report		
REP06284W0	ACTION (Form PCT/ISA/220) as well as, where applicable, item 5 below.			
International application No.	International filing date (day/month/year)	(Earliest) Priority Date (day/month/year)		
PCT/GB 99/04013	01/12/1999	01/12/1998		
Applicant				
ENDOCRINE PHARMACEUTICALS	LIMITED et al.	-		
This International Search Report has been according to Article 18. A copy is being tra	n prepared by this International Searching Auth ansmitted to the International Bureau.	nority and is transmitted to the applicant		
This International Search Report consists  [X] It is also accompanied by	of a total of2 sheets. a copy of each prior art document cited in this	report.		
Basis of the report				
<ul> <li>a. With regard to the language, the interpretation language in which it was filed, unlended.</li> </ul>	international search was carried out on the bas ess otherwise indicated under this item.	sis of the international application in the		
the international search was Authority (Rule 23.1(b)).	as carried out on the basis of a translation of th	ne international application furnished to this		
b. With regard to any nucleotide and/or amino acid sequence disclosed in the international application, the international search was carried out on the basis of the sequence listing:  contained in the international application in written form.  filed together with the international application in computer readable form.  furnished subsequently to this Authority in written form.				
	furnished subsequently to this Authority in computer readble form.			
the statement that the sub-	subsequently furnished written sequence listing does not go beyond the disclosure in the on as filed has been furnished.			
	formation recorded in computer readable form is identical to the written sequence listing has been			
2. Certain claims were foun	nd unsearchable (See Box I).			
3. Unity of Invention is lack	ding (see Box II).			
4. With regard to the title,				
X the text is approved as sub	omitted by the applicant.			
the text has been establish	ned by this Authority to read as follows:			
		•		
5. With regard to the abstract,				
the text is approved as sub the text has been establish within one month from the	omitted by the applicant. ned, according to Rule 38.2(b), by this Authority date of mailing of this international search repo	y as it appears in Box III. The applicant may,		
6. The figure of the <b>drawings</b> to be publis		or, sabilities to this Authority.		
as suggested by the applic	· · · · · · · · · · · · · · · · · · ·	X None of the figures.		
because the applicant faile				
because this figure better of	characterizes the invention.			



In	ilonal	Application No
PCI	/GB	99/04013

A CLASS	FICATION OF SUBJECT MATTER		,		
IPC 7	A61K35/16				
λ.					
According	to International Patent Classification (IPC) or to both national cla	ssification and IPC			
B. FIELDS	SEARCHED				
Minimum d	ocumentation searched (classification system followed by classi	fication symbols)			
IPC 7	A61K				
i					
Documenta	ation searched other than minimum documentation to the extent t				
Doodinena	rance extend of roughly and minimum under the real version to the extent	nat such documents are included in the fields se	earched		
Electronic o	data base consulted during the international search (name of dat	a base and, where practical search terms used	)		
1			•		
[ ] [ ] [	ternal, WPI Data, PAJ, BIOSIS, ME	DLINE, CHEM ABS Data, SCI	SEARCH		
			•		
i					
C DOCUM	ENTS CONSIDERED TO BE RELEVANT				
Category °	Citation of document, with indication, where appropriate, of th	e relevant passages	Relevant to claim No.		
Α	HART JE: "Pituitary-related we	eight	1-9		
	changes affecting the liver, ut	terus and			
	adrenal glands of rats treated	with			
	hexoestrol and clomiphene in hi	igh doses"			
	TOXICOLOGY,	·			
	vol. 61, no. 2,				
	17 April 1990 (1990-04-17), pages 185-94,				
	XP000929158				
	cited in the application the whole document	ł			
	the whole document				
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İ					
Furth	er documents are listed in the continuation of box C.	Patent family members are listed in	annex.		
° Special cate	egories of cited documents:				
		"T" later document published after the intern	national filing date		
"A" documer conside	nt defining the general state of the art which is not ered to be of particular relevance	or priority date and not in conflict with the cited to understand the principle or theo	ne application but by underlying the		
"E" earlier do	ocument but published on or after the international	invention "X" document of particular relevance; the cla	imad investiga		
filing da "L" documen	ite It which may throw doubts on priority_claim(s) or	cannot be considered novel or cannot b	e considered to		
which is	cited to establish the publication date of another	involve an inventive step when the docu "Y" document of particular relevance; the cla			
	or other special reason (as specified)  nt referring to an oral disclosure, use, exhibition or	cannot be considered to involve an inve	ntive step when the		
other m	eans	document is combined with one or more ments, such combination being obvious	to a person skilled		
"P" documen later tha	nt published prior to the international filing date but on the priority date claimed	in the art.  "&" document member of the same patent far	mile.		
	ctual completion of the international search				
+ at	sampled of the line had old Sedicti	Date of mailing of the international search	ch report		
12	July 2000	27/07/2000			
10	cary 2000	27/07/2000			
Name and ma	ailing address of the ISA	Authorized officer			
	European Patent Office, P.B. 5818 Patentlaan 2 NL – 2280 HV Rijswijk				
	Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Stein, A			
	· 45. (TO 1-70) 040-00 ID	Joe 111, A	i		

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# WORLD INTELLECTUAL PROPERTY ORGANIZATION International Bureau



# INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(21) International Application Number: PCT/GB99/04013 (81) Des	esignated States: AE, AL, AM, AT, AU, AZ, BA, BB, BG.
(30) Priority Data: 9826186.0 1 December 1998 (01.12.98) GB  (71) Applicant (for all designated States except US): ENDOCRINE PHARMACEUTICALS LIMITED [GB/GB]; 19 Herbert Street, Hemel Hempstead, Herts HP2 5HP (GB).  (72) Inventor; and (75) Inventor/Applicant (for US only): HART, John, Ernest [GB/GB]; 19 Herbert Street, Old Town, Hemel Hempstead, Herts HP2 5HP (GB).	BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG US, UZ, VN, YU, ZA, ZW, ARIPO patent (GH, GM, KE LS, MW, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM GA, GN, GW, ML, MR, NE, SN, TD, TG).

#### (57) Abstract

A material having the ability to reduce organ mass has been isolated by collecting ovarian venous blood from a female mammal; preparing ovarian venous plasma from the blood; and at least partially purifying said material from the plasma. This material has therapeutic and other uses, e.g. in the treatment of organ or tissue hypertrophy.

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EE	Estonia	LR	Liberia	SG			
				50	Singapore		





**Ional Application No** PCT/GB 99/04013

A. CLASSI IPC 7	FICATION OF SUBJECT MATTER A61K35/16					
According to	o International Patent Classification (IPC) or to both national classification and IPC					
	SEARCHED					
IPC 7	cumentation searched (classification system followed by classification symbols) A61K					
Documenta	ion searched other than minimum documentation to the extent that such documents are inclu	ided in the fields searched				
Electronic d	ata base consulted during the international search (name of data base and, where practical	search terms used)				
	ternal, WPI Data, PAJ, BIOSIS, MEDLINE, CHEM ABS	·				
	, , , , , , , , , , , , , , , , , , , ,	July 3010E/Moli				
C. DOCUM	ENTS CONSIDERED TO BE RELEVANT					
Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.				
		Florovatilit to classif \$40.				
A	HART JE: "Pituitary-related weight	1-9				
	changes affecting the liver, uterus and					
	adrenal glands of rats treated with					
	hexoestrol and clomiphene in high doses" TOXICOLOGY.					
	vol. 61, no. 2,					
	17 April 1990 (1990-04-17), pages 185-94,					
	XP000929158					
	cited in the application the whole document					
	the whole document					
		; 				
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		nembers are listed in annex.				
* Special cat	egories of cited documents : T* later document publi	shed after the international filing date				
"A" docume conside	nt defining the general state of the art which is not of pnormy date and cited to understance cited to understance	not in conflict with the application but the principle or theory underlying the				
'E' earlier d	E* earlier document but published on or after the international filter date.  *X* document of particular relevance: the claimed invention					
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another.  cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone						

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another

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# INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

A - liver the or agentic file reference				
Applicant's or agent's file reference	FOR FURTHER ACT		eation of Transmittal of International y Examination Report (Form PCT/IPEA/416)	
REP06284WO				
International application No.				
PCT/GB99/04013	01/12/1999		01/12/1998	
International Patent Classification (IPC) or n A61K35/16	ational classification and IPC		·	
Applicant				
ENDOCRINE PHARMACEUTICAL	S LIMITED et al.			
This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.				
2. This REPORT consists of a total o	f 5 sheets, including this	cover sheet.		
<ul> <li>This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).</li> <li>These annexes consist of a total of sheets.</li> </ul>				
This report contains indications rel	ating to the following item	s:		
│ │ │ │ │ │ │ Basis of the report				
II 🗆 Priority				
III   Non-establishment of	opinion with regard to nov	elty, inventive step	and industrial applicability	
IV ☐ Lack of unity of invent	ion			
	under Article 35(2) with re- ions suporting such stater		rentive step or industrial applicability;	
VI □ Certain documents ci				
VII   Certain defects in the	international application			
VIII   Certain observations of	on the international applica	ation		
Date of submission of the demand		Date of completion of	f this report	
21/06/2000		18.08.2000		
Name and mailing address of the internation	nal	Authorized officer	aches mo	

preliminary examining authority:

Furonean Patent Office

# INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/GB99/04013

#### I. Basis of the report

1.	resp	ils report has been drawn on the basis of (substitute sheets which have been furnished to the receiving Office h sponse to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to e report since they do not contain amendments.):				
	D s	cription, pages:				
	1-9		as originally filed			
	Clai	ims, No.:				
	1-9		as originally filed			
	Dra	wings, sheets:				
	1/3-	3/3	as originally filed			
2.	The	amendments have	e resulted in the cancellation of:			
		the description,	pages:			
		the claims,	Nos.:			
		the drawings,	sheets:			
3.			een established as if (some of) the amendments had not been made, since they have been beyond the disclosure as filed (Rule 70.2(c)):			

4. Additional observations, if necessary:



International application No. PCT/GB99/04013

- V. Reasoned stat m nt und r Articl 35(2) with regard to nov lty, inventive st p or industrial applicability; citations and xplanations supporting such statement
- 1. Statement

Novelty (N)

Yes:

Claims 1-9

Claims 1-9

No:

Claims

Inventive step (IS)

Yes: No:

Claims

Industrial applicability (IA)

Yes:

Claims 1-9

No: Claims

2. Citations and explanations

see separate sheet

#### INTERNATIONAL PRELIMINARY **EXAMINATION REPORT - SEPARATE SHEET**

#### Re Item V

Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Reference is made to the following document:

D1: Hart J.E.: TOXICOLOGY, vol. 61, no. 2, 1990, pages 185-94

- 2. Claims 1-9 meet the requirements of Art. 33(2) and 33(3) PCT because their subject matter is new and inventive over the prior art cited in the search report (see below).
- 2.1 D1 which is the only prior art document cited in the search report, represents the closest prior art. As acknowledged in the application, D1 (see e.g. abstract), discloses that clomiphene antagonises the ability of the oestrogen hexoestrol to increase the organ weight of several organs in female rats.
- 2.2 The present invention relates to a material containing at least partially purified ovarian venous plasma prepared from ovarian venous blood from a female mammal, and to the use of said material for the treatment of organ or tissue hypertrophy.
- 2.3 The principle underlying the subject matter of the present claims is based on the finding that an endogenous material obtained by at least partially purifying ovarian venous plasma prepared from ovarian venous blood from a female mammal can diminish the size and weight of many organs and tissues throughout the body. [Said finding is supported by the experimental data of the present application].
- 2.4 Since nothing in D1 teaches or suggests the existence of such a endogenous material, the subject matter of the present
  - claims 1-7 (which are directed to the aforementioned material);
  - claim 8 (which is directed to a pharmaceutical composition comprising said material); and

# INTERNATIONAL PRELIMINARY

International application No. PCT/GB99/04013

**EXAMINATION REPORT - SEPARATE SHEET** 

(iii) claim 9 (which is directed to the use of said material for the treatment of hypertrophy)

is considered to be new and inventive.

Claims 1-9 satisfy the criterion set forth in Art. 33(4) PCT because their subject 3. matter is susceptible of industrial application.